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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/757,824	01/09/2001	Beverly L. Davidson	875.043US1	8235

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EXAMINER	
YAEN, CHRISTOPHER H	
ART UNIT	PAPER NUMBER
1642	25

DATE MAILED: 09/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/757,824	DAVIDSON ET AL.	
	Examiner	Art Unit	
	Christopher H Yaen	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 August 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *36-48 and 63-78* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *36-48 and 63-78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *26* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/19/2003 has been entered.

2. The amendment after final filed 4/11/2003 is hereby acknowledged and entered into the record. Accordingly, claims 1-35 and 49-61 are canceled and claims 63-78 are newly added.

3. Therefore, claims, 36-48 and 62-78 are pending and examined on the merits.

Claim Rejections Maintained - 35 USC § 103

4. The rejection of claims 36-48 and 62-78 under 35 USC 103(a) is maintained for the reasons of record. Applicant argues that because original claim 36 was never rejected, it was assumed to be free of the prior art. However, upon further review and reconsideration, the newly amended claims are still obvious over the prior art cited. In the response filed 4/11/2003 (paper no. 18, page 6), applicant states "many kits are commercially available for the artisans to easily generate fusion proteins [.]" and that "it is quite routine for artisans to generate fusion proteins." Applicant previously argued that the references must teach the limitations of the claims or provide sufficient

motivation to make the instantly claimed invention. Schwarze *et al* teach a fusion protein comprising a Tat PTD, more specifically Tat_{47-57}, fused to a FITC molecule and or β-galactasidase (β-gal). It is also taught by Schwarze *et al* that the expression product of the fusion construct was able to localize in the brain. Although it is not specifically recited in the Schwarze *et al* reference, one of ordinary skill would have found it obvious to at the time the invention was made to conjugate/fuse *any* protein to the Tat PTD in view of the fact that over 50 proteins have already been conjugated to the Tat PTD (see page 1570). Furthermore, by applicant's own admission, those of skill in the art have available to them many kits that aid in the construction of fusion proteins and that construction is considered routine (see page 6 of paper no. 18). As such, the generation of a lysosomal enzyme conjugated to a PTD would also be considered routine and obvious to one of ordinary skill. The skilled artisan would have used the β-Glucuronidase cDNA of Ghodsi *et al* (see page 2332, 2nd column first paragraph) and substituted the FITC and or β-gal taught by Schwarze *et al* with the gene encoding β-Glucoronidase. Schwarze *et al* provides sufficient motivation to do so because more than 50 different proteins ranging in size have already been fused to the Tat PTD (see page 1570). Therefore one of skill in the art would expect a reasonable amount of success in fusing just about *any* protein to the Tat PTD in view of the statements taught in Schwarze *et al*. The *in situ* expression of the claimed fusion peptide in the brain of a patient is an intended usage of the claimed product as does not read any patentable weight into the claims.

New Arguments

Claim Rejections - 35 USC § 112, 1st paragraph

(Written Description)

5. Claims 36,37, 39-48, and 62-78 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The following *written description* rejection is set forth herein.

The claims recite a "soluble lysosomal enzymes", "naturally secreted proteins" (i.e. growth factors or anti-neoplastic proteins), "nuclear proteins", and "cytoplasmic proteins" as part of the invention. However, there does not appear to be an adequate written description in the specification as-filed of the essential structural feature that provides the recited function of any and all soluble lysosomal enzymes, naturally secreted proteins (i.e. growth factors or anti-neoplastic proteins), nuclear proteins, and cytoplasmic proteins. The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a

combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 3rd column).

Applicant does not appear to have reduced to practice all soluble lysosomal enzymes, or any naturally secreted proteins (i.e. growth factors or anti-neoplastic proteins), nuclear proteins, and cytoplasmic proteins. Neither has Applicant provided a sufficient written description of all soluble lysosomal enzymes or any naturally secreted proteins (i.e. growth factors or anti-neoplastic proteins), nuclear proteins, and cytoplasmic proteins structure that may be correlated with the species of β-Glucuronidase. A "soluble lysosomal enzyme" encompasses *any* molecule with the functional activity of acid hydrolyzing complex chemicals in the body. Thus the genus of compounds encompassed by this term is extensive and the artisan would not be able to recognize that Applicant was in possession of the invention as now claimed.

Consequently, Applicant was not in possession of the instant claimed invention. See Regents of the University of California v. Eli Lilly and Co. 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). Adequate written description of genetic material "'requires a precise definition, such as by structure, formula, chemical name, or physical properties,' not a mere wish or plan for obtaining the claimed chemical invention." Id. 43 USPQ2d at 1404 (quoting Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606). The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter of the claim. Id. 43 USPQ2d at 1406. A description of what the genetic material does, rather than of what it is, does not suffice. Id.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001. Applicant is invited to point to clear support or specific examples of the claimed invention in the specification as-filed.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 36, 39, 45, 47, 48, 62, 63, 65-67, 70, 71, 76, and 78 are rejected under 35 U.S.C. 102(b) as being anticipated by Schwarze *et al* (previously cited). Claims are drawn to a polypeptide comprising a soluble lysosomal enzyme (claim 36), a naturally secreted protein (claim 39), a cytoplasmic protein (claim 45) operably linked to a PTD (claims 36,66,70), wherein the PTD is a Tat PTD (claim 47), more specifically Tat_{47-57} (claim 48, 67,71). The claims are further limited to the said polypeptides being enzymatically active (claims 62,63, and 65) and biologically active (claims 73 and 78).

Schwarze *et al* teach a Tat_{47-57} PTD-β-galactosidase fusion protein (see page 1571 column 1, 1st full paragraph), which was both enzymatically and biologically active (see page 1571, 3rd full paragraph). The specification defines Tat_{47-57} as having the following amino acid sequence YGRKKRRQRRR (see figure 1a). Schwarze *et al* also

uses the same Tat PTD sequence (see 1572, item 7 under **References and Notes** section).

It is well established that β-galactosidase is a lysosomal enzyme (as evidenced by the fact that lysosomal enzymes are defined as an acid hydrolase see www.ggc.org/diagnostic/biochemical/lysosomal_enzymes.htm -copy enclosed) that is secreted (as evidenced by Blum JJ *et al* J. Cell Physiol 1975 Aug;86(1):131-42) and expressed in the cytoplasm (as evidenced by Emr *et al* Mol. Cell Biol. 1984 Nov;4(11):2347-2355). The specification defines soluble lysosomal enzymes as enzymes which are secreted (see page 3 line 21). Therefore, it is inherent that the β-galactosidase taught by Schwarze *et al* would also have the properties of being a soluble and secreted protein and also characterized as a cytoplasmic protein.

All other rejections are withdrawn in view of the amendments and arguments thereto as set forth in Paper No. 18.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Christopher Yaen
Art Unit 1642
September 12, 2003

ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600